The roles of non-coding RNAs in the self-renewal and differentiation of pluripotent stem cells

Grant Award Details

The roles of non-coding RNAs in the self-renewal and differentiation of pluripotent stem cells

Grant Type: New Faculty II

Grant Number: RN2-00923

Project Objective: The objective of this project is to identify the role of non-coding RNAs in the self-renewal and differentiation of pluripotent stem cells.

Investigator:

Name:	Lin He
Institution:	University of California, Berkeley
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $1,406,823

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Reporting Period: Year 5

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: The roles of non-coding RNAs in the self-renewal and differentiation of pluripotent stem cells

Public Abstract: There are thousands of cell types in the animal body, many of which can be derived from embryonic stem cells (ES cells), a pluripotent cell type that thrive in cell culture condition. ES cells differentiate into various cell type in a tissue culture dish in response to different growth factor/cytokine treatment, which can be transplanted back into animals for regenerative medicine application. In recent years, scientists have generated another type of pluripotent stem cell population, designated as induced pluripotent stem cells (iPS cells). These iPS cells are derived from adult cell types, and capable of differentiating into a variety of cell types in a tissue culture dish. Both ES cells and iPS cells not only provide a unique paradigm to study early mammalian development, but also hold great promise for regenerative medicine. Therefore, understanding the molecular network that regulate stem cell maintenance and stem cell differentiation of these cell types are very important for their application in regenerative medicine. In the studies we proposed, we will examine a novel class of gene regulators for their functions to maintain the stem cell population, as well as to trigger their differentiation into specific lineages. The focus of our studies is non-coding RNAs, which are RNA molecules that do not have capacity to encode proteins. Among the best studied non-coding RNAs are the microRNAs, which are small RNA molecules that are potent regulator for gene expression. These small RNAs often have the capacity to each regulate hundred of genes, therefore, regulating diverse developmental processes and physiological processes. If the biogenesis of these small RNAs are removed, stem cells exhibit multiple defects both in the tissue culture dish and in animal development. In this proposal, we aim to investigate the roles of non-coding RNAs in the regulation of stem cell maintenance and differentiation, and to identify novel non-coding RNA regulators that may impact stem cell biology. It is worth noting that RNA therapies, particularly those using synthetic small RNAs or their inhibitors, bypass the need for conventional gene therapy, and provide great promise for clinical application. The methods to delivery small RNAs into the cells and animals have been improved significantly over the past decade, and it is very likely that small RNAs and their inhibitors will be soon utilized for therapeutic applications. Therefore, our proposed research will generate exciting findings to stem cell biology and may lead to the development of novel diagnostic markers and therapeutic approaches for regenerative medicine.

Statement of Benefit to California:	The studies proposed here explore the functions of novel non-coding RNAs in the self-renewal and differentiation in pluripotent stem cells. This is a new area of stem cell research, which, in funded, can benefit the state of the California to develop new diagnostic markers and therapeutic approaches in regenerative medicine. to gain knowledge on the molecular basis for pluripotency, and to train young scientists in stem cell biology. In what follows, the benefit of proposed research to the State of California and its citizens are summarized in details. Pluripotent stem cells not only provide a unique paradigm to study early mammalian development, but also hold great promise for regenerative medicine. RNA therapies are an area of intense investigation, and the in vitro and in vivo delivery methods for RNA molecules have been greatly improved over the past few years. Therefore, it is possible in the near future to use RNA therapy, particularly those involving small RNAs or their inhibitors, for regenerative medicine. RNA therapy is fundamentally different from the “conventional” growth factor or cytokine delivery to modulate stem/progenitor cells. RNA therapy by itself, or in combination with conventional therapy, may provide a novel approach for regenerative medicine. In addition, studies of non-coding RNAs in stem cells may give rise to new markers for stem cells, as well as their differentiated lineages. The proposed research will carefully examine the roles of non-coding RNAs in regulating the pluripotency of stem cells, which is a field in its infancy. Not only the knowledge acquired from this study will enhance our understanding on the molecular basis for stem cell maintenance and differentiation, but the novel research tools developed from this study will also benefit the stem cell research in the state of California and its people. In addition, the proposed research will allow young scientists to be well trained in the stem cell field, and to combine two exciting fields in biology, i.e., non-coding RNA biology and stem cell biology. And such training will be critical for the state of California to have its own research force on stem cell biology in the future.